12 August 2015
EMA/COMP/430728/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Synthetic double-stranded RNA oligonucleotide specific to hydroxyacid oxidase 1 gene for the treatment of primary hyperoxaluria type 1

On 28 July 2015, orphan designation (EU/3/15/1528) was granted by the European Commission to Dicerna EU Limited, United Kingdom, for synthetic double-stranded RNA oligonucleotide specific to hydroxyacid oxidase 1 gene for the treatment of primary hyperoxaluria type 1.

What is primary hyperoxaluria type 1?

Primary hyperoxaluria type 1 is an inherited disease caused by the lack of a liver enzyme called alanine-glyoxylate aminotransferase (AGXT). This enzyme is needed to convert a substance called glyoxylate into glycine, an amino acid used for making enzymes and other proteins. Patients who lack this enzyme have high levels of oxalate in the urine, because glyoxylate instead of being converted into glycine is converted into excess oxalate. Oxalate can form calcium oxalate deposits, which can cause stones in the kidney and urinary tract (structures that carry urine) as well as injury to other organs such as the heart, eyes, bones and skin. Characteristic symptoms of the disease include blood in the urine, tummy pain and frequent urinary tract infections.

Primary hyperoxaluria type 1 is long-term debilitating and life threatening because of the high rate of kidney failure seen with the condition.

What is the estimated number of patients affected by the condition?

At the time of designation, primary hyperoxaluria type 1 affected less than 0.1 in 10,000 people in the European Union (EU). This was equivalent to fewer than 5,000 people*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU for treating primary hyperoxaluria type 1. Different treatments were used to prevent the accumulation of calcium oxalate

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 512,900,000 (Eurostat 2015).

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such as dietary changes, drinking plenty of fluids and taking vitamin B_6. Kidney and liver transplantation have been possible options in certain cases.

How is this medicine expected to work?

This medicine is expected to reduce the body's production of glyoxylate, the substance that is converted to oxalate in patients with primary hyperoxaluria type 1. Normally, production of glyoxylate is regulated by an enzyme called hydroxyacid oxidase (also known as glycolate oxidase). The medicine is designed to attach specifically to genetic material in the cell responsible for the production of hydroxyacid oxidase. This blocks production of the enzyme so that less glyoxylate is created, thereby reducing the production of oxalate. Therefore, the chance of forming calcium oxalate deposits is reduced.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with the medicine in patients with primary hyperoxaluria type 1 had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for primary hyperoxaluria type 1 or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 18 June 2015 recommending the granting of this designation.

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Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information

Sponsor's contact details:

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For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Synthetic double-stranded RNA oligonucleotide specific to hydroxyacid oxidase 1 gene	Treatment of primary hyperoxaluria type 1
Bulgarian	Синтетичен двойно-верижен РНК олигонуклеотид специфичен за гена на хидрокси киселата оксидаза тип 1	Лечение на първична хипероксалурия тип 1
Croatian	Sintetski dvolančani oligonukleotid RNK specifičan za gen za hidroksi kiselina oksidazu 1	Liječenje primarne hiperoksalurije tipa 1
Czech	Syntetický dvou vláknový RNA oligonukleotid specifický pro gen hydroxyacid oxigenázy 1	Léčba primární hyperoxalurie typu 1
Danish	Syntetisk dobbelt-strenget RNA oligonucleotid specifikt til hydroxysyre oxidase 1 gen	Behandling af primær hyperoxaluri type 1
Dutch	Synthetisch dubbelstrengig RNA oligonucleotide specifiek voor hydroxyzuuroxidase-1-gen	Behandeling van primaire hyperoxalurie type 1
Estonian	*Hydroxyacid oxidase* 1 geeni spetsiifiline sünteetiline kaheahelaline RNA oligonukleotiid	1. tüüpi esmase hüperoksaluuria ravi
Finnish	Synteettinen kaksoiskierteinen RNA oligonukleotidi, joka on spesifinen hykroksihapon oksidaasi 1:n geenille	Tyypin 1 primaarisen hyperoksalurian hoito
French	Oligonucléotide synthétique ARN double brin spécifique du gene hydroxyacide oxidase 1	Traitement de l'hyperoxalurie primaire de type 1
German	Synthetisches doppelsträngiges RNA-Oligonukleotid spezifisch für das Hydroxyazid Oxydase 1 Gen	Behandlung der primären Hyperoxalurie Typ 1
Greek	Συνθετικό δίκλωνο ολιγονουκλεοτίδιο RNA ειδικό για το γονίδιο της υδροξυοξεϊκής οξειδάσης 1	Θεραπεία της πρωτοπαθούς υπεροξαλουρίας τύπου 1
Hungarian	Hydroxyacid oxidáz 1 génre specifikus szintetikus kettős szálú RNS oligonukleotid	Az 1-es típusú, primer hiperoxaluria kezelésére
Italian	Oligonucleotide sintetico di RNA a doppia catena speciifico per il gene ossidasi idrossiacida 1	Trattamento delll'iperossaluria primaria di tipo 1
Latvian	Hidroksi skābes oksidāzes 1 gēnam specificsks sintētisks dubulspirāļu RNS oligonukleotīds	1. tipa primāras hiperoksalūrijas ārstēšana
Lithuanian	Sintetinis dvigrandis RNR oligonukleotidas, specifiškas hidroksirūgšties oksidazės 1 genui	Pirminės hiperoksalurijos, I tipo, gydymas
Maltese	Oligonukleotide sintetiku tar-RNA b'katina doppja speċifiku għall-ġene hydroxyacid oxidase 1	Kura ta' iperoxalurja primarja tip 1
Polish	Syntetyczny dwuniciowy oligonukleotyd RNA specyficzny dla genu oksydazy hydroksykwasów 1	Leczenie pierwotnej hiperoksalurii typu I
Portuguese	Oligonucleótido sintético de cadeia dupla de ARN específico do gene da hidroxiácido oxidase	Tratamento da hiperoxalúria primária de tipo 1
Romanian	Oligonucleotid sintetic ARN dublu-spiralat specific pentru gena hidroxiacid oxidazei 1	Tratamentul hiperoxaluriei primare de tip 1

[1] At the time of designation

Language	Active ingredient	Indication
Slovak	Syntetický dvojvláknový RNA oligonukleotid špecifický ku génu hydroxyacid oxidázy 1	Liečba primárnej hyperoxalúrie typu 1
Slovenian	Sintetični dvojno verižni RNK oligonukleotid specifičen za hidroksi oksidazni 1 gen	Zdravljenje primarne hiperoksalurije vrste 1
Spanish	Oligonucleótido sintético de RNA de doble cadena específico del gen de hidroxiácido oxidasa 1	Tratamiento de la hiperoxaluria primaria de tipo 1
Swedish	Syntetisk dubbelsträngad RNA oligonukleotid specifik för hydroxysyra oxidase 1 gen	Behandling av primär hyperoxaluri typ 1
Norwegian	Syntetisk dobbeltrådet RNA oligonukleotid spesifikk for hydroxysyre oxidase 1 genet	Behandling av primær hyperoksaluri type 1.
Icelandic	Tilbúið tvístrengja RNA ólígónúkleótíð sértækt fyrir hýdroxýsýru oxidasa 1 gen	Meðferð við fyrsta stigs sólarhringsútskilnaði >0,49 mmól (hyperoxaluria), af gerð 1